REMARKS

Claims 61 and 66 are pending in the subject application. Applicants have not added, cancelled or amended any claims herein.

Rejections under 35 U.S.C. §112, First Paragraph

Written Description

The Examiner stated that claims 61 and 66 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner alleged that the original application does not provide adequate support for the broadly claimed genus of antagonists that are capable of abrogating HIV-1 infection by binding to the CCR5 chemokine receptor. The Examiner asserted, *inter alia*, that "a small number of β-chemokines were identified with inhibitory activity (e.g., the β-chemokines MIP-Iα and -1β)" and that "two chemokine antagonists, met-RANTES and MCP-1(Δ1-8), might be useful in the claimed methodology." The Examiner also stated that "Although the specification does provide a small number of inhibitory agents, nevertheless, this limited number of species is insufficient to place the inventors in possession of the full genus of agents at the time of filing."

In response, applicants respectfully traverse the Examiner's rejection.

Contrary to the Examiner's remarks, applicants note that the specification in fact discloses a large number of inhibitory agents. Applicants note that MCP-1(Δ1-8) is actually eight different compounds (see page 27, lines 22-24). As other examples of CCR5 chemokine

antagonists, the specification also discloses chemokines with N-terminal deletions (see page 27, lines 20-22). In addition, the specification discloses met-RANTES, (see page 27, lines 12-13 and 29-32, as well as four different deletions of the SDF-1 polypeptide (see page 16, lines 37-38). The specification also describes fragments of chemokine (see page 16, lines 4-5) and chemokines with deletions (see page 16, lines 6-9, for example) as well as modified chemokines (see page 16, lines 21-25). Multiple other antagonists based on SDF-1 are also disclosed (see page 17, lines 1 to 10). Antibodies and portions thereof are also disclosed (see page 17, lines 11-12). Furthermore, nonpeptidyl agents are disclosed at page 17, line 13. Moreover, the specification provides guidance regarding agents that are not useful in the claimed invention, for example, naturally occurring chemokines (see page 13, lines 37-38), bicyclams and their derivatives (see page 14, lines 6-7), and those chemokine fragments and derivatives which activate leukocyte responses (see page 26, lines 35-37) or inflammatory responses (see page 27, line 15-18). Accordingly, in contrast to the Examiner's position, multiple generic and specific agents are described, including chemokine-based agents, polypeptides, antibodies and non-peptidyl agents.

With regard to the Examiner's comments on written description as to biomolecules and function thereof, as stated on page 5 of the Office Action, applicants further note they are <u>not</u> claiming a genus of biomolecules. Rather, the invention as claimed herein is a <u>method</u>, and the present claims relate to a genus of the method described, and not to a genus of biomolecules. Applicants further note that if the specification conveys to one skilled in the relevant art that applicants were in possession of the claimed *method*, then the written description rejection should be withdrawn. Moreover, as described in MPEP 2163, even in a situation where actual compounds were being claimed, "'The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes' where the genes were novel combinations

of known DNA segments", citing Capon v. Eshar, 418 F.3d at 1358, 76 USPQ2d at 1084. (Emphasis added).

In the present case, as disclosed, for example, on page 27, lines 5-9 and 25-27, chemokine antagonists were known in the art. In addition to the known antagonists, applicants have described many more types of inhibitory molecules in the specification as detailed above. Moreover, applicants have specified the subgenus of CCR5 chemokine antagonists that bind specifically to the CCR5 chemokine receptor on the surface of the CD4+ cell; block fusion of HIV-1_{JR-FL} with a PM-1 cell; do not block fusion of HIV-1_{BRU} with such PM-1 cell; and do not activate an inflammatory response upon binding to the CCR5 chemokine receptor on the surface of the CD4+ cell. Accordingly, applicants maintain that one of ordinary skill in the art would recognize applicants to be in possession of the invention as claimed.

Applicants further maintain that the specification discloses the relationship between the physical/chemical properties and the function of the claimed CCR5 chemokine receptor antagonists. As explained starting on page 36, line 17 of the instant specification, CCR5 (also known as C-C CKR-5) is the co-receptor, which, with CD4, is needed for HIV-1 entry into a cell. At page 36, lines 20-22, the specification states that "[i]t has been known for a decade that HIV-1 requires a second receptor for entry into CD4+ cells". Also, as stated on page 36, lines 35-37, and as shown on page 37, Table 3, "[t]he expression of C-C CKR-5 on Hela-CD4 (human), COS-CD4 (simian) and 3T3-CD4 (murine) cells rendered each of them readily infectible by the primary, NSI strains ADA and BaL in the env-complementation assay of HIV-1 entry." Accordingly, applicants submit that the specification discloses that HIV-1 requires two receptors for entry into a CD4+ cell, the second receptor being CCR5, and that the blocking of HIV-1 gp120 binding to CCR5 would inhibit entry of HIV-1 into a CD4+ cell. Thus, applicants maintain that one skilled in the art would understand the physical and chemical properties of the CCR5 chemokine receptor antagonists that enable them to bind to the CCR5 chemokine receptor on

the surface of a CD4+ cell, and to block fusion of a CD4+ cell with a macrophage-tropic HIV-1, but not with a T-cell tropic HIV-1, which are particularly disclosed properties of such antagonists. Accordingly, applicants maintain that the specification clearly describes the correlation between the identifying properties and the function of the CCR5 chemokine receptor antagonist as recited in the claimed methods.

In view of the foregoing remarks, applicants maintain that the specification satisfies the written description requirement of 35 U.S.C. §112, first paragraph, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Enablement

The Examiner rejected claims 61 and 66 under 35 U.S.C. §112, first paragraph, asserting that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with the claims. The Examiner stated that the claims of the application are "broadly directed to any antagonist that is capable of abrogating HIV-1 infection through CCR5 binding interactions." The Examiner also asserted that the disclosure provides a generic in vitro resonance energy transfer (RET) screening assay that enables the skilled artisan to detect HIV-1 fusion events, but that this "method by itself does not lead the skilled artisan to any particular class of compounds."

In response, applicants respectfully traverse the Examiner's rejection. Initially, applicants note that a "particular class of compounds" is not being claimed herein, and enablement of such is not the issue. Furthermore, the Examiner's statement on page 11 of the Office Action that the claims of the application are "broadly directed to any antagonist that is capable of abrogating HIV-1 infection through CCR5 binding interactions" is wrong. In fact, the claimed method recites contacting a CD4+ cell with one subgenus of CCR5 chemokine receptor antagonists having particular properties, i.e. a

subgenus which binds specifically to the CCR5 chemokine receptor on the surface of the CD4+ cell; blocks fusion of HIV-1_{JR-FL} with a PM-1 cell; does not block fusion of HIV-1_{BRU} with such PM-1 cell; and does not activate an inflammatory response upon binding to the CCR5 chemokine receptor on the surface of the CD4+ cell.

Applicants also describe how to identify such antagonists in the specification. As the Examiner has acknowledged on page 12 of the Office Action, an RET assay is provided. This RET assay does not simply identify *any* chemokine antagonist, instead it specifically identifies CCR5 chemokine receptor antagonists with the properties recited in claim 61. Applicants maintain that the RET assay disclosed is not merely a generic methodology. Based on applicants' disclosure, one skilled in the art can readily perform the RET screening assay as described to identify those chemokine receptor antagonists having the properties that are recited in claim 61 and new claim 66. Applicants note that one skilled in the art is also provided with working examples in which this assay was used to identify a number of CCR5 chemokine receptor antagonists with the claimed properties (see, for example, pages 35-36, Table 2a and Table legend).

In addition, applicants note that the specification discloses at page 15, lines 12-24, a second method for identifying CCR5 chemokine receptor antagonists. Specifically, the specification discloses the following assay as a method of identifying CCR5 chemokine receptor antagonists: 1) incubating soluble CD4 with biotinylated gp120 from HIV-1_{JR-FL}; 2) incubating this complex with CCR5-expressing cells that do not express CD4 in the presence or absence of a candidate chemokine receptor antagonist; 3) washing and incubating with streptavidin-phycoerythrin; and 4) washing and measuring the amount of bound gp120 using a flow cytometer or fluorometer; and 5) calculating the degree of inhibition of binding by the candidate chemokine receptor antagonist. Accordingly, applicants maintain that the instant specification provides a written description of CCR5 chemokine receptor antagonists and describes specific methodology that enables the skilled person in the art to

identify such CCR5 chemokine receptor antagonists so as to adequately establish applicants' possession of the claimed invention.

Applicants further note that the Examiner concluded, reciting various rationales, that "it would clearly require undue experimentation from the skilled artisan to practice the claimed invention."

In response to the Examiner's statements, applicants maintain that 'some' experimentation is not necessarily synonymous with "undue experimentation". In fact, "[t]he test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976)." (See MPEP 2164.01). With regard to how to make the claimed invention, as far as this applies to methods, applicants have described hereinabove how one of skill in the art can readily apply the RET assay described in the specification to identify members of the disclosed subgenus of CCR5 receptor antagonists.

With regard to using the claimed invention, as far as this applies to methods, applicants note that MPEP 2164.01(c) states that "it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. 112, first paragraph." Based on the foregoing, applicants submit that one of ordinary skill in the art would be able to make and use the invention as claimed.

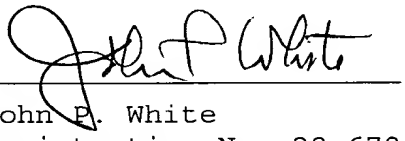
In view of the foregoing remarks, applicants maintain that one skilled in the art would have readily been able to make and use applicants' claimed invention based on the subject disclosure in view of the knowledge in the art at the time. Accordingly, applicants maintain that the specification satisfies the enablement requirement of 35 U.S.C.

§112, first paragraph, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the total enclosed fee of $960.00, including a $405.00 Request for Continued Examination ("RCE") fee and a $555.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Communication and RCE. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited on this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

3/19/09

John P. White Date
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